

Substitute for form 1449B-PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

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Sheet 1 of 15

**Complete if Known**

Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 <del>1015</del> / 6 23
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

**NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T <sup>2</sup>
me	1	ABRAHAM et al. "Synthesis and biological activity of aromatic amino acid phosphoramidates of 5-fluoro-2'-deoxyuridine and 1-β-arabinofuranosylcytosine: Evidence of phosphoramidase activity" <i>J. Med. Chem.</i> (1996) 39:4569-4575	
	2	AKDAS et al. "Glutathione S-transferase and multidrug-resistant phenotype in transitional cell carcinoma of the bladder" <i>Eur. Urol.</i> (1996) 29(4):483-486	
	3	ALMASAN et al. "Genetic instability as a consequence of inappropriate entry into and progression through S-phase" <i>Cancer Metast. Rev.</i> (1995) 14:59-73	
	4	ANDERSEN et al. "Detection of C-ERBB-2 related protein in sera from breast cancer patients" <i>Acta. Oncol.</i> (1995) 34(4):499-504	
	5	ANGLADA et al. "N,N-cyclization of carbodiimides with 2-(bromomethyl)acrylic acid. A direct entry to the system 5-methylene-6H-pyrimidine-2,4-dione, A new class of thymine analogues" <i>J. Heterocyclic Chem.</i> (July-Aug. 1996) 33:1259-1270	
	6	ANTELMAN et al. "Inhibition of tumor cell proliferation in vitro and in vivo by exogenous p110 <sup>RB</sup> , the retinoblastoma tumor suppressor protein" <i>Oncogene</i> (1995) 10:697-704	
	7	ASAKURA and ROBINS, "Cerium(IV) catalyzed iodination at C5 of uracil nucleosides" <i>Tetrahedron Lett.</i> (1988) 29(23):2855-2858	
	8	ASAKURA and ROBINS "Cerium(IV)-mediated halogenation at C-5 of uracil derivatives" <i>J. Org. Chem.</i> (1990) 55:4928-4933	
	9	ARISI et al. "Comparison of the antiviral effects of 5-methoxymethyldeoxyuridine-5'-monophosphate with adenine arabinoside-5'-monophosphate" <i>Antivir. Res.</i> (1983) 3:161-174	
	10	BAGSHAWE "Antibody-directed enzyme prodrug therapy: A review", <i>Drug Develop. Res.</i> (1995) 34(2):220-230	
	11	BAJETTA et al. "A pilot safety study of capecitabine, a new oral fluoropyrimidine, in patients with advanced neoplastic disease" <i>Tumori</i> (1996) 82:450-452	
	12	BALZARINI et al. "Incorporation of 5-substituted pyrimidine nucleoside analogues into DNA of a thymidylate synthetase-deficient murine FM3A carcinoma cell line" <i>Meth. Find. Exp. Clin. Pharmacol.</i> (1985) 7(1):19-28	
me	13	BALZARINI et al. "Thymidylate synthase is the principal target enzyme for the cytostatic activity of (E)-5-(2-bromovinyl)-2'-deoxyuridine against murine mammary carcinoma (FM3A) cells transformed with the herpes simplex virus type 1 or type 2 thymidine kinase gene" <i>Mol. Pharmacol.</i> (1987) 32:410-416	

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Signature

L. E. Crane

Date  
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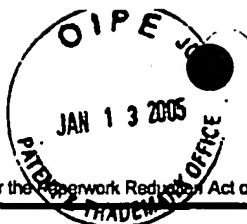
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Sheet 2 of 15

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Art Unit	1623 <del>1615</del> 1623
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

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JEC	14	BALZARINI et al. "Differential mechanism of cytostatic effect of (E)-5-(2-bromovinyl)-2'-deoxyuridine, 9-(1,3-dihydroxy-2-propoxymethyl)guanine, and other antihertic drugs on tumor cells transfected by the thymidine kinase gene of herpes simplex virus type 1 or type 2" <i>J. Biol. Chem.</i> (1993) 268(9):6332-6337	
	15	BALZARINI et al. "Anti-HIV and anti-HBV activity and resistance profile of 2',3'-dideoxy-3'-thiacytidine (3TC) and its arylphosphoramidate derivative CF 1109" <i>Biochem. Biophys. Res. Co.</i> (1996) 225:363-369	
	16	BALZARINI et al. "Conversion of 2',3'-dideoxyadenosine (ddA) and 2',3'-dideoxy-2',3'-dideoxyadenosine (d4A) to their corresponding arylphosphoramidate derivatives markedly potentiates their activity against human immunodeficiency virus and hepatitis B virus" <i>FEBS Lett.</i> (1997) 410:324-328	
	17	BANERJEE et al. "Molecular mechanisms of resistance to antifolates, a review" <i>Acta Biochim. Pol.</i> (1995) 42(4):457-464	
	18	BANERJEE et al. "Role of E2F-1 in chemosensitivity" <i>Cancer Res.</i> (Oct. 1, 1998) 58:4292-4296	
	19	BARBATO, et al. "Synthesis of bridged pyrimidine nucleosides and triazo [4,3-c] pyrimidine nucleoside analogues" <i>Nucleos. Nucleot.</i> (1991) 10(4):853-866	
	20	BARBOUR et al. "A naturally occurring tyrosine to histidine replacement at residue 33 of human thymidylate synthase confers resistance to 5-fluoro-2'-deoxyuridine in mammalian and bacterial cells" <i>Mol. Pharmacol.</i> (1992) 42:242-248	
	21	BARR "Inhibition of thymidylate synthetase by 5-alkynyl-2'-deoxyuridylates" <i>J. Med. Chem.</i> (1981) 24(12):1385-1388	
	22	BARR et al. "Thymidylate synthetase-catalyzed conversions of E-5-(2-bromovinyl)-2'-deoxyuridylate" <i>J. Biol. Chem.</i> (1983) 258(22):13627-13631 (Nov. 25, 1983)	
	23	BARR et al. "Reaction of 5-ethynyl-2'-deoxyuridylate with thiols and thymidylate synthetase" <i>Biochemistry</i> (1983) 22:1696-1703	
	24	BARRETT "Trapping of the C5 methylene intermediate in thymidylate synthase" <i>J. Am. Chem. Soc.</i> (1998) 120:449-450	
JEC	25	BENZARIA et al. "Synthesis, <i>in vitro</i> antiviral evaluation, and stability studies of bis(S-acyl-2-thioethyl) ester derivatives of 9-[2-(phosphonomethoxy)ethyl]adenine (PMEA) as potential PMEA prodrugs with improved oral bioavailability" <i>J. Med. Chem.</i> (1996) 39:4958-4965	

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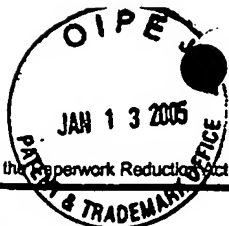
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Sheet 3 of 15

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First Named Inventor	H. Michael SHEPARD
Art Unit	1623 --1615--
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

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Me	26	BERGSTROM et al. "C-5-substituted pyrimidine nucleosides. 3. Reaction of allylic chlorides, alcohols, and acetates with pyrimidine nucleoside derived organopalladium intermediates" <i>J. Org. Chem.</i> (1981) 46(7):1432-1441	
Me	27	BERGSTROM et al. "Synthesis of (E)-5-(3,3,3-trifluoro-1-propenyl)-2'-deoxyuridine and related analogues: Potent and unusually selective antiviral activity of (E)-5-(3,3,3-trifluoro-1-propenyl)-2'-deoxyuridine against herpes simplex virus type 1" <i>J. Med. Chem.</i> (1984) 27:279-284	
Me	28	BERKOW et al. (eds); <i>The Merck Manual of Diagnosis and Therapy</i> , 16th Edition, Merck & Co., Rahway, NJ, (May 1992) only page 1278 supplied	
Me	29	BERTINO et al. "Resistance mechanisms to methotrexate in tumors" <i>Stem Cells</i> (1996) 14:5-9	
Me	30	BIGGE et al. "Palladium-catalyzed coupling reactions of uracil nucleosides and nucleotides" <i>J. Amer. Chem. Soc.</i> (Mar. 12, 1980) 102(6):2033-2038	
Me	31	BLACKLEDGE "New developments in cancer treatment with the novel thymidylate synthase inhibitor raltitrexed ('Tomudex')" <i>British J. Cancer</i> (1998) 77(Supp 2):29-37	
Me	32	BOSSLET et al. "A novel one-step tumor-selective prodrug activation system" <i>Tumor Targeting</i> (1995) 1:45-50	
Me	33	BOSSLET et al. "Elucidation of the mechanism enabling tumor selective prodrug monotherapy" <i>Cancer Res.</i> (Mar 15, 1998) 58:1195-1201	
Me	34	BRISON "Gene amplification and tumor progression" <i>Biochim. Biophys. Acta</i> (1993) 1155:25-41	
Me	35	CARL et al. "Protease-activated 'prodrugs' for cancer chemotherapy" <i>PNAS USA</i> (April 1980) 77(4):2224-2228	
Me	36	CARRERAS and SANTI "The catalytic mechanism and structure of thymidylate synthase" <i>Annu. Rev. Biochem.</i> (1995) 64:721-762	
Me	37	CARTER et al. "Humanization of an anti-p185 <sup>HER2</sup> antibody for human cancer therapy" <i>PNAS USA</i> (May 1992) 89:4285-4289	
Me	38	CAVA and LEVINSON "Thionation reactions of Lawesson's reagents" <i>Tetrahedron</i> (1985) 41(22):5061-5087	
Me	39	CHAKRAVARTY et al. "Plasmin-activated prodrugs for cancer chemotherapy. 2. Synthesis and biological activity of peptidyl derivatives of doxorubicin" <i>J. Med. Chem.</i> (1983) 26(5):638-644	
Me	40	CHAUDHURI and KOOL "Very high affinity DNA recognition by bicyclic and cross-linked oligonucleotides" <i>J. Am. Chem. Soc.</i> (1995) 117:10434-10442	

Examiner's  
Signature

L. E. Crane

Date  
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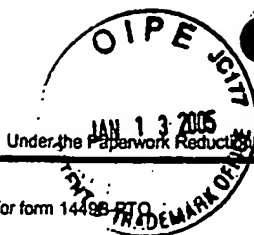
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		Filing Date	November 28, 2002		
		First Named Inventor	H. Michael SHEPARD		
		Art Unit	1623 ---1615---		
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JEC	41	CHEN et al. "Sensitization of human breast cancer cells to cyclophosphamide and ifosfamide by transfer of a liver cytochrome P450 gene" <i>Cancer Res.</i> (Mar. 15, 1996) 56:1331-1340		
	42	CHO and JOHNSON "(E)-5-(3-oxopropen-1-yl)-2'-deoxyuridine and (E)-5-(3-oxopropen-1-yl)-2',3'-dideoxyuridine; New antiviral agents: Synthesis and biological activity" <i>Tetrahedron Lett.</i> (1994) 35(8):1149-1152		
	43	CLARKE "Animal models of breast cancer: Their diversity and role in biomedical research" <i>Breast Cancer Res. Tr.</i> (1996) 39:1-6		
	44	CODERRE et al. "Mechanism of action of 2',5-difluoro-1-arabinosyluracil" <i>J. Med. Chem.</i> (1983) 26(8):1149-1152		
	45	COLACINO "Mechanisms for the anti-hepatitis B virus activity and mitochondrial toxicity of fialuridine (FIAU)" <i>Antivir. Res.</i> (1996) 29:125-139		
	46	COLLINS et al. "Sulicide prodrugs activated by Thymidylate synthase: Rationale for treatment and noninvasive imaging of tumors with deoxyuridine analogues" <i>Clin. Cancer Res.</i> (August 1999) 5:1976-1981		
	47	CONNORS "Prodrugs in cancer chemotherapy" <i>Xenobiotica</i> (1986) 16(10/11):975-988		
	48	CONNORS "Is there a future for cancer chemotherapy?" <i>Ann. Oncol.</i> (1996) 7:445-452		
	49	CONNORS and KNOX "Prodrugs in cancer chemotherapy" <i>Stem Cells</i> (1995) 13:501-511		
	50	COPUR et al. "Thymidylate synthase gene amplification in human colon cancer cell lines resistant to 5-fluorouracil" <i>Biochem. Pharmacol.</i> (1995) 49(10):1419-1426		
JEC	51	CRISP "Synthesis of 5-alkenyl-2'-deoxyuridines via organostannanes" <i>Synth. Commun.</i> (1989) 19(11 & 12):2117-2123		
	52	DAGLE et al. "Targeted degradation of mRNA in Xenopus oocytes and embryos directed by modified oligonucleotides: Studies of An2 and Cyclin in embryogenesis" <i>Nucleic Acids Res.</i> (Aug. 25, 1990) 18(16):4751-4757		
JEC	53	DALE et al. "The synthesis and enzymatic polymerization of nucleotides containing mercury: Potential tools for nucleic acid sequencing and structural analysis" <i>PNAS USA</i> (August 1973) 70(8):2238-2242		
	54	DAVISSON et al. "Expression of human thymidylate synthase in <i>Escherichia coli</i> " <i>J. Biol. Chem.</i> (1989) 264(16):9145-9148		
JEC	55	DAVISSON et al. "Expression of human thymidylate synthase in <i>Escherichia coli</i> . (Additions and corrections)" <i>J. Biol. Chem.</i> (Dec. 2, 1994) 269(48):30740		
Examiner's Signature	L. E. Crane <i>[Signature]</i>		Date Considered	09/21/2005

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<i>See</i>	56	DeCLERCQ et al. "Nucleic acid related compounds. 40. Synthesis and biological activities of 5-alkynyluracil nucleosides" <i>J. Med. Chem.</i> (1983) 26:661-666	
	57	DICKER et al. "Methotrexate resistance in an <i>in vivo</i> mouse tumor due to a non-active-site dihydrofolate reductase mutation" <i>PNAS USA</i> (Dec. 1993) 90:11797-11801	
	58	DIRVIN et al. "The role of human glutathione S-transferase isoenzymes in the formation of glutathione conjugates of the alkylating cytostatic drug thiotepa" <i>Cancer Res.</i> (April 15, 1995) 55:1701-1706	
	59	DORR and von HOFF "PALA" In: <i>Cancer Chemotherapy Handbook</i> , 2nd Edition, Appleton & Lange, Norwalk, Connecticut (1994) pp. 768-773	
	60	DUNN, III et al. "Solution of the conformation and alignment tensors for the binding of trimethoprim and its analogs to dihydrofolate reductase: 3D-quantitative structure-activity relationship study using molecular shape analysis, 3-way partial least-squares regression, and 3-way factor analysis" <i>J. Med. Chem.</i> (1996) 39:4825-4832	
	61	DYER et al. "Nucleic Acids Chemistry: Improved and new synthetic procedures, methods, and techniques" Townsend, L. B. & Tipson, R. S., eds. (Wiley-Interscience, New York, NY) (1991) 4:79-83	
	62	ECCLES et al. "Significance of the c-erbB family of receptor tyrosine kinases in metastatic cancer and their potential as targets for immunotherapy" <i>Invasion Metastasis</i> (1994-95) 14(1-6):337-348	
<i>See</i>	63	EISENBRAND et al. "An approach towards more selective anticancer agents" <i>J. Synthetic Organic Chem.</i> (1996) 10:1246-1258	
**	64	EVARD et al. "An <i>in vitro</i> nucleoside analog screening method for cancer gene therapy" <i>Cell Biol. Toxicol.</i> (1996) 12:345-350	
<i>See</i>	65	EVARD et al. "An <i>in vitro</i> nucleoside analog screening method for cancer gene therapy" <i>Chem. Abstracts</i> (1996) 126:Abstract No. 26514	
	66	FARQUHAR et al. "Synthesis and antitumor evaluation of bis[(pivaloyloxy)methyl] 2'-deoxy-5-fluorouridine 5'-monophosphate (FdUMP): A strategy to introduce nucleotides into cells" <i>J. Med. Chem.</i> (1994) 37:3902-3909	
	67	FARQUHAR et al. "5'-[4-pivaloyloxy]-1,3,2-dioxaphosphorinan-2-yl]-2'-deoxy-5-fluorouridine: A membrane-permeating prodrug of 5-fluoro-2'-deoxyuridylic acid (FdUMP)" <i>J. Med. Chem.</i> (1995) 38:488-495	
	68	FARRUGIA et al. "Single agent infusional 5-fluorouracil is not effective second-line therapy after raltitrexed (Tomudex®) in advanced colorectal cancer" <i>Eur. J. Cancer</i> (1998) 34(7):987-991	
	69	FELIP et al. "Overexpression of c-erbB-2 in epithelial ovarian cancer" <i>Cancer</i> (Apr. 15, 1995) 75(8):2147-2152	
<i>See</i>	70	FINCH "Radiation Injury" In: <i>Harrison's Principles of Internal Medicine</i> , 12th Edition, McGraw-Hill, Inc., New York, NY (1991) 2204-2208	

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Attorney Docket Number	NB 2006.01

## NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T <sup>2</sup>
<i>[Signature]</i>	71	FINER-MOORE et al. "Refined structures of substrate-bound and phosphate-bound thymidylate synthase from <i>Lactobacillus casei</i> " <i>J. Mol. Biol.</i> (1993) 232:1101-1116	
<i>[Signature]</i>	72	FINER-MOORE et al. "Crystal structure of thymidylate synthase from T4 phage: Component of a deoxynucleoside triphosphate-synthesizing complex" <i>Biochemistry</i> (1994) 33:15459-15468	
<i>[Signature]</i>	73	<del>FIRESTONE et al. "A comparison of the effects of antitumor agents upon normal human epidermal keratinocytes and human squamous cell carcinoma" <i>J. Invest. Dermatol.</i> (May 1990) 94(5):657-661</del>	
<i>[Signature]</i>	74	FIRESTONE et al. "A comparison of the effects of antitumor agents upon normal human epidermal keratinocytes and human squamous cell carcinoma" <i>Chem Abstracts</i> (1990) 113:Abstract No. 254	
<i>[Signature]</i>	75	FREED et al. "Evidence for acyloxymethyl esters of pyrimidine 5'-deoxyribonucleotides as extracellular sources of active 5'-deoxyribonucleotides in cultured cells" <i>Biochem. Pharmacol.</i> (1989) 38(19):3193-3198	
<i>[Signature]</i>	76	FRIES et al. "Synthesis and biological evaluation of 5-fluoro-2'-deoxyuridine phosphoramidate analogs" <i>J. Med. Chem.</i> (1995) 38(14):2672-2680	
<i>[Signature]</i>	77	GARRETT et al. "Thymidylate synthetase. Catalysis of dehalogenation of 5-bromo-and 5-iodo-2'-deoxyuridylate" <i>Biochemistry</i> (1979) 18(13):2798-2804	
<i>[Signature]</i>	78	GOLDBERG et al. "Novel cell imaging techniques show induction of apoptosis and proliferation in mesothelial cells by asbestos" <i>Am. J. Respir. Cell Mol. Biol.</i> (1997) 17:265-271	
<i>[Signature]</i>	79	GOLDSTEIN and BROWN "Genetic aspects of disease" <i>In: Harrison's Principles of Internal Medicine</i> , 12th Edition, McGraw-Hill, Inc., New York, NY (1991) pp. 21-76	
<i>[Signature]</i>	80	GOODWIN et al. "Incorporation of alkylthiol chains at C-5 of deoxyuridine" <i>Tetrahedron Lett.</i> (1993) 34(35):5549-5552	
<i>[Signature]</i>	81	GOTTESMANN et al. "Genetic analysis of the multidrug transporter" <i>Annu. Rev. Genet.</i> (1995) 29:607-649	
<i>[Signature]</i>	82	GRAHAM et al. "DNA duplexes stabilized by modified monomer residues: Synthesis and stability" <i>J. Chem. Soc. Perkin Trans.</i> (1998) 1:1131-1138	
<i>[Signature]</i>	83	GROS et al. "Isolation and expression of a complementary DNA that confers multidrug resistance" <i>Nature</i> (Oct. 1986) 323:728-731	
<i>[Signature]</i>	84	GROS et al. "Mammalian multidrug resistance gene: Complete cDNA sequence indicates strong homology to bacterial transport proteins" <i>Cell</i> (Nov. 7, 1986) 47:371-380	
<i>[Signature]</i>	85	GROS et al. "Isolation and characterization of DNA sequences amplified in multidrug-resistant hamster cells" <i>PNAS USA</i> (Jan. 1986) 83:337-341	
<i>[Signature]</i>	86	GUDKOV et al. "Cloning and characterization of DNA sequences amplified in multidrug-resistant djungarian hamster and mouse cells" <i>Somat. Cell Mol. Genet.</i> (1987) 13(6):609-619	

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Sheet 7 of 15

## Complete if Known

Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 --1615--
Examiner Name	Not Yet Assigned
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<i>See</i>	87	HANFIELD and LEVESQUE "Strategies for isolation of in vitro expressed genes from bacteria" <i>FEMS Microbiol. Revs.</i> (1999) 23:69-91	
**	88	HAKIMELAH et al. "Design, synthesis and structure-activity relationship of novel dinucleotide analogs as agents against herpes and human immunodeficiency viruses" <i>J. Med. Chem.</i> (Nov. 10, 1995) 38(23):4648-4659	
<i>See</i>	89	HARDY et al. "Atomic structure of thymidylate synthase: Target for rational drug design" <i>Science</i> (Jan. 23, 1987) 235:448-455	
	90	HARRIS et al. "Adenovirus-mediated p53 gene transfer inhibits growth of human tumor cells expressing mutant p53 protein" <i>Cancer Gene Ther.</i> (1996) 3(2):121-130	
	91	HASHIMOTO et al. "Simple separation of tritiated water and [³H]deoxyuridine from [5-³H]deoxyuridine 5'-monophosphate in the thymidylate synthase assay" <i>Anal. Biochem.</i> (1987) 167:340-346	
	92	HEIDELBERGER et al. "Fluorinated pyrimidines and their nucleosides" <i>Adv. Enzymol. Related Areas Mol. Biol.</i> (1983) 54:57-119	
	93	HENGSTSCHLAGER et al. "The role of p16 in the E2F-dependent thymidine kinase regulation" <i>Oncogene</i> (1996) 12:1635-1643	
	94	HOBBS, Jr. "Palladium-catalyzed synthesis of alkynylamino nucleosides. A universal linker for nucleic acids" <i>J. Org. Chem.</i> (1989) 54:3420-3422	
	95	HORIKOSHI et al. "Quantitation of thymidylate synthase, dihydrofolate reductase, and DT-diaphorase gene expression in human tumors using the polymerase chain reaction" <i>Cancer Res.</i> (Jan. 1, 1992) 52:108-116	
	96	HORN et al. "Fialuridine is phosphorylated and inhibits DNA synthesis in isolated rat hepatic mitochondria" <i>Antivir. Res.</i> (1997) 34:71-74	
	97	HOSTETLER et al. "Enhanced oral absorption and antiviral activity of 1-O-octadecyl-sn-glycero-3-phospho-acyclovir and related compounds in hepatitis B virus infection, <i>in vitro</i> " <i>Biochem. Pharmacol.</i> (1997) 53:1815-1822	
	98	HOUE, et al. "Detection of thymidylate synthase gene expression levels in formalin-fixed paraffin embedded tissue by semiquantitative, nonradioactive reverse transcriptase polymerase chain reaction" <i>Tumor Biol.</i> (1997) 18:53-68	
<i>See</i>	99	HSAIO and BARDOS "Synthesis of 5'-thymidyl bis(1-aziridinyl)phosphinates as antineoplastic agents" <i>J. Med. Chem.</i> (1981) 24:887-889	

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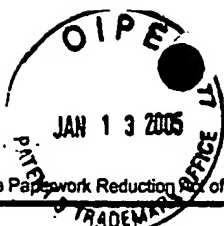
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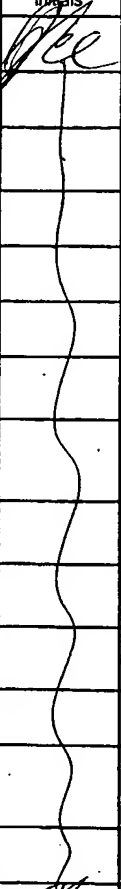
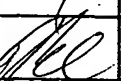
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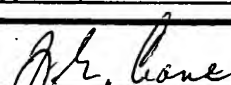
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First Named Inventor	H. Michael SHEPARD
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	100	HU et al. "Determination of absorption characteristics of AG337, a novel thymidylate synthase inhibitor, using a perfused rat intestinal model" <i>J. Pharmaceutical Sciences</i> (July 1998) <b>87(7):886-890</b>	
	101	HUANG and SANTI "Active site general catalysts are not necessary for some proton transfer reactions of thymidylate synthase" <i>Biochemistry</i> (1997) <b>36:1869-1873</b>	
	102	HUDZIAK et al. "Amplified expression of the HER2/ERBB2 oncogene induces resistance to tumor necrosis factor $\alpha$ in NIH 3T3 cells" <i>PNAS USA</i> (July 1988) <b>85:5102-5106</b>	
	103	HUDZIAK et al. "Selection for transformation and met protooncogene amplification in NIH 3T3 fibroblasts using tumor necrosis factor $\alpha$ " <i>Cell Growth &amp; Differentiation</i> (1990) <b>1:129-134</b>	
	104	HUSAK et al. "Pseudotumour of the tongue caused by herpes simplex virus type 2 in an HIV-1 infected immunosuppressed patient" <i>Brit. J. Dermatol.</i> (1998) <b>139:118-121</b>	
	105	IMAI et al. "Studies on phosphorylation. IV. Selective phosphorylation of the primary hydroxyl group in nucleosides" <i>J. Org. Chem.</i> (June 1969) <b>34(6):1547-1550</b>	
	106	JACKMAN et al. "Quinazoline-based thymidylate synthase inhibitors: Relationship between structural modifications and polyglutamation" <i>Anti-Cancer Drug Design</i> (1995) <b>10:573-589</b>	
	107	JOHNSTON et al. "Production and characterization of monoclonal antibodies that localize human thymidylate synthase in the cytoplasm of human cells and tissue" <i>Cancer Res.</i> (Dec. 15, 1991) <b>51:6668-6676</b>	
	108	JOHNSTON "The role of thymidylate synthase expression in prognosis and outcome of adjuvant chemotherapy in patients with rectal cancer" <i>J. Clin. Oncol.</i> (Dec. 1994) <b>12(12):2640-2647</b>	
	109	KAMB "Cyclin-dependent kinase inhibitors and human cancer" <i>Curr. Top. Microbiol. Immunol.</i> (1998) <b>227:139-148</b>	
	110	KASHANI-SABET et al. "Detection of drug resistance in human tumors by <i>in vitro</i> enzymatic amplification" <i>Cancer Res.</i> (Oct. 15, 1988) <b>48:5775-5778</b>	
	111	KATKI et al. "Prodrugs activated by thymidylate synthase: Treatment of tumors with deoxyuridine analogs" <i>Proc. Amer. Assoc. Cancer Res.</i> (March 1998) <b>39:Abstract No. 1275</b>	
	112	KLECKER et al. "Toxicity, metabolism, DNA incorporation with lack of repair, and lactate production for 1-(2'-fluoro-2'-deoxy- $\beta$ -D-arabinofuranosyl)-5-iodouracil in U-937 and MOLT-4 cells" <i>Mol. Pharmacol.</i> (1994) <b>46:1204-1209</b>	
	113	KNIGHTON et al. "Structure of and kinetic channelling in bifunctional dihydrofolate reductase-thymidylate synthase" <i>Nature Struct. Biol.</i> (March 1994) <b>1(3):186-194</b>	
	114	KOBAYASHI et al. "Effect of hammerhead ribozyme against human thymidylate synthase on the cytotoxicity of thymidylate synthase inhibitors" <i>Jpn. J. Cancer Res.</i> (Nov. 1995) <b>86:1014-1018</b>	

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JPC	115	KODAMA et al. "Evaluation of antiherpetic compounds using a gastric cancer cell line: Pronounced activity of BVDU against herpes simplex virus replication" <i>Microbiol. Immunol.</i> (1996) 40(5):359-363	
	116	KUMAR et al. "Synthesis and biological evaluation of some cyclic phosphoramidate nucleoside derivatives" <i>J. Med. Chem.</i> (Sept. 1990) 33(9):2368-2374	
	117	KUNDU et al. "Synthesis and biological activities of [E]-5-(2-acylvinyl) uracils" <i>Eur. J. Med. Chem.</i> (1993) 28:473-479	
	118	KUROBOSHI and HIYAMA "A facile synthesis of difluoromethylene compounds by oxidative fluorodesulfurization of dithioacetals using tetrabutylammonium dihydrogentrifluoride and N-halo compounds" <i>SYNLETT</i> (Dec. 1991) pp. 909-910	
	119	KUROBOSHI and HIYAMA "A facile synthesis of $\alpha,\alpha$ -difluoroalkyl ethers and carbonyl fluoride acetals by oxidative desulfurization-fluorination" <i>SYNLETT</i> (April 1994) pp. 251-252	
	120	LAM "Application of combinatorial library methods in cancer research and drug discovery" <i>Anti-Cancer Drug Design</i> (1997) 12:145-167	
	121	LARSSON et al. "Thymidylate synthase in advanced gastrointestinal and breast cancers" <i>Acta Oncologica</i> (1996) 35(4):469-472	
	122	LASIC "Doxorubicin in sterically stabilized liposomes" <i>Nature</i> (Apr. 11, 1996) 380:561-562	
	123	LEWIS et al. "A serum-resistant cytofection for cellular delivery of antisense oligodeoxynucleotides and plasmid DNA" <i>PNAS USA</i> . (April 1996) 93:3176-3181	
	124	LI et al. "Lack of functional retinoblastoma protein mediates increased resistance to antimetabolites in human sarcoma cell lines" <i>PNAS USA</i> (Oct. 1995) 92:10436-10440	
	125	LIN et al., "Rhenium188 hydroxyethylidene diphosphonate: a new generator-produced radiotherapeutic drug of potential value for the treatment of bone metastases" <i>Eur. J. Nucl. Med.</i> 24(6):590-595 (June 1997)	
	126	LIVAK et al. "Detection of single base differences using biotinylated nucleotides with very long linker arms" <i>Nucl. Acids Res.</i> (1992) 20(18):4831-4837	
127	LIVINGSTONE et al. "Altered cell cycle arrest and gene amplification potential accompany loss of wild-type p53" <i>Cell</i> (Sept. 18, 1992) 70:923-935		
128	LÖNN et al. "Higher frequency of gene amplification in breast cancer patients who received adjuvant chemotherapy" <i>Cancer</i> (Jan. 1, 1996) 77(1):107-112		
ME	129	LOVEJOY et al. "Animal models and the molecular pathology of cancer" <i>J. Pathol.</i> (1997) 181:130-135	

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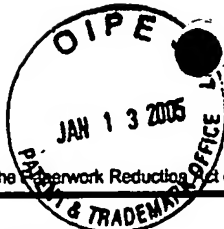
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	130	MASTERS and ALTARDI "The nucleotide sequence of the cDNA coding for the human dihydrofolate acid reductase" <i>Gene</i> (1983) 21:59-63	
	131	McGUIGAN et al. "Certain phosphoramidate derivatives of dideoxy uridine (ddU) are active against HIV and successfully by-pass thymidine kinase" <i>FEBS Lett</i> (1994) 351:11-14	
	132	McGUIGAN "Aryl phosphate derivatives of AZT retain activity against HIV1 in cell lines which are resistant to the action of AZT" <i>Antivir. Res.</i> (1992) 17:311-321	
	133	McGUIGAN "Intracellular delivery of bioactive AZT nucleotides by aryl phosphate derivatives of AZT" <i>J. Med. Chem.</i> (1993) 36:1048-1052	
	134	McGUIGAN "Aryl phosphoramidate derivatives of d4T have improved anti-HIV efficacy in tissue culture and may act by the generation of a novel intracellular metabolite" <i>J. Med. Chem.</i> (1996) 39:1748-1753	
	135	McGUIGAN et al. "Synthesis and evaluation of some masked phosphate esters of the anti-herpetic drug 882C (netivudine) as potential antiviral agents" <i>Antivir. Chem. Chemoth.</i> (1998) 9:233-243	
	136	McINTEE "Probing the mechanism of action and decomposition of amino acid phosphomonoester amidates of antiviral nucleoside prodrugs" <i>J. Med. Chem.</i> (1997) 40:3323-3331	
	137	McKAY et al. "Broad spectrum aminoglycoside phosphotransferase type III from <i>Enterococcus</i> : Overexpression, purification, and substrate specificity" <i>Biochemistry</i> (1994) 33:6936-6944	
	138	MEAD et al. "Pharmacologic aspects of homofolate derivatives in relation to amethopterin-resistant murine leukemia" <i>Cancer Res.</i> (Nov. 1966) 26(1):2374-2379	
	139	MEDEN et al. "Elevated serum levels of a c-erbB-2 oncogene product in ovarian cancer patients and in pregnancy" <i>J. Cancer Res. Clin. Oncol.</i> (1994) 120:378-381	
	140	MEIER et al. "ADA-bypass by lipophilic cyclosal-ddAMP pro-nucleotides a second example of the efficiency of the cyclosal-concept" <i>Bioorg. Med. Chem. Lett.</i> (1997) 7(12):1577-1582	
	141	MEIER et al. "Cyclic saligenyl phosphotriesters of 2',3'-dideoxy-2',3'-didehydrothymidine (d4T) - a new pro-nucleotide approach" <i>Bioorg. Med. Chem. Lett.</i> (1997) 7(2):99-104	
	142	MEIER et al. "CycloSal-pro-nucleotides: The design and biological evaluation of a new class of lipophilic nucleotide prodrugs" <i>Int'l. Antiviral News</i> (1997) 5(10):183-185	
	143	MELTON et al. "Antibody-directed enzyme prodrug therapy (ADEPT). Review article" <i>Drugs of the Future</i> (1996) 21(2):167-181	
	144	MELTON and SHERWOOD "Antibody-enzyme conjugates for cancer therapy" <i>J. Natl. Cancer Inst.</i> (Feb. 21, 1996) 88(3/4):153-165	
	145	MIDGLEY and KERR "Colorectal cancer" <i>Lancet</i> (Jan 30, 1999) 353:391-399	

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10/048,033 - PTO-1449 #3

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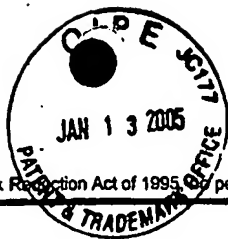
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Substitute for form 1449B-PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)		<b>Complete if Known</b>	
		Application Number	10/048,033
		Filing Date	November 28, 2002
		First Named Inventor	H. Michael SHEPARD
		Art Unit	1623 <del>==1615==</del>
		Examiner Name	Not Yet Assigned
Sheet 11 of 15	Attorney Docket Number	NB 2006.01	

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T <sup>2</sup>
<i>[Signature]</i>	146	MONTFORT and WEICHSEL "Thymidylate synthase: Structure, inhibition, and strained conformations during catalysis" <i>Pharmacol. Ther.</i> (1997) 76(1-3):29-43	
<i>[Signature]</i>	147	MONTGOMERY et al., "Phosphonate analogue of 2'-deoxy-5-fluorouridylic acid" <i>J. Med. Chem.</i> (1979) 22(1):109-111	
<i>[Signature]</i>	148	MORGAN et al. "Tumor efficacy and bone marrow-sparing properties of TER286, a cytotoxin activated by glutathione S-transferase" <i>Cancer Res.</i> (June 15, 1998) 58:2568-2575	
<i>[Signature]</i>	149	MORRISON & BOYD (eds) <i>Organic Chemistry</i> , Allyn & Bacon, Inc., Boston, MA, (1973) only pages 1170-1180 supplied	
<i>[Signature]</i>	150	MURAKAMI and SEKIYA "Accumulation of genetic alterations and their significance in each primary human cancer and cell line" <i>Mutat. Res.</i> (1998) 400(1-2):421-437	
<i>[Signature]</i>	151	NAESENS et al. "Anti-HIV activity and metabolism of phosphoramidate derivatives of D4T-MP with Variations in the amino acid moiety" Poster Session 1, <u>The Tenth International Conference on Antiviral Research</u> , Hotel Nikko, Atlanta, GA April 6-11, 1997; published in <i>Antivir. Research</i> (April 1997) 34(2):A54 (Abstract 40)	
<i>[Signature]</i>	152	NAKANO et al., "Critical role of phenylalanine 34 of human dihydrofolate reductase in substrate and inhibitor binding and in catalysis" <i>Biochemistry</i> (1994) 33:9945-9952	
<i>[Signature]</i>	153	NICHOL and HAKALA "Comparative growth-inhibitory activity of homofolic acid against cell lines sensitive and resistant to amethopterin" <i>Biochem. Pharmacol.</i> (Oct. 1966) 15(10):1621-1623	
<i>[Signature]</i>	154	NOOTER and STOTER "Molecular mechanisms of multidrug resistance in cancer chemotherapy" <i>Path. Res. Pract.</i> (1996) 192:768-780	
<i>[Signature]</i>	155	OSAKI et al. "5-fluorouracil (5-FU) induced apoptosis in gastric cancer cell lines: Role of the p53 gene" <i>Apoptosis</i> (1997) 2:221-226	
<i>[Signature]</i>	156	OSHIRO et al. "Genotoxic properties of (E)-5-(2-bromovinyl)-2'-deoxyuridine (BVDU)" <i>Fundam. Appl. Toxicol.</i> (1992) 18:491-498	
<i>[Signature]</i>	157	PARDO et al. "The incorporation of deoxyuridine monophosphate in DNA increases the sister-chromatid exchange yield" <i>Exp Cell Res.</i> (1987) 168:507-517	
<i>[Signature]</i>	158	PARK et al. "Chemotherapy efficacy of E-5-(2-bromovinyl)-2'-deoxyuridine for orofacial infection with herpes simplex virus type 1 in mice" <i>J. Infectious Diseases</i> (June 1982) 145(6):909-913	
<i>[Signature]</i>	159	PERRY et al. "Plastic adaptation toward mutations in proteins: Structural comparison of thymidylate synthases" <i>Proteins</i> (1990) 8:315-333	
<i>[Signature]</i>	160	PESTALOZZI et al. "Prognostic importance of thymidylate synthase expression in early breast cancer" <i>J. Clin. Oncol.</i> (May 1997) 15(5):1923-1931	
Examiner's Signature	L. E. Crane <i>[Signature]</i>		Date Considered
			09/21/2005

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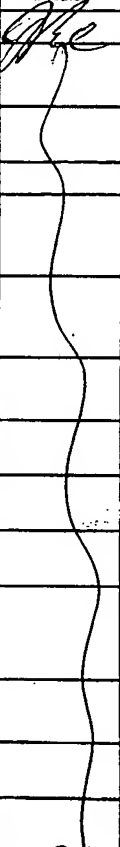
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Sheet 12 of 15

**Complete if Known**

Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 --1615--
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

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	161	PETERS et al. "Thymidylate synthase and drug resistance" <i>Eur. J. Can.</i> (1995) 31A(7/8):1299-1305	
	162	PHELPS et al. "Synthesis and biological activity of 5-fluoro-2'-deoxyuridine 5'-phosphorodiamidates" <i>J. Med. Chem.</i> (1980) 23:1229-1232	
	163	PUPA et al. "The extracellular domain of the c-erbB-2 oncoprotein is released from tumor cells by proteolytic cleavage" <i>Oncogene</i> (1993) 8:2917-2923	
	164	ROBERTS "An isotopic assay for thymidylate synthetase" <i>Biochemistry</i> (Nov. 1966) 5(11):3546-3548	
	165	ROBINS and BARR "Nucleic acid related compounds. 31. Smooth and efficient palladium-copper catalyzed coupling of terminal alkynes with 5-iodouracil nucleosides" <i>Tetrahedron Lett.</i> (1981) 22:421-424	
	166	ROBINS et al. "Nucleic acid related compounds. 38. Smooth and high-yield iodination and chlorination at C-5 of uracil bases and p-toluy-protected nucleosides" <i>Can. J. Chem.</i> (1982) 60:554-557	
	167	ROBINS and BARR "Nucleic acid compounds. 39. Efficient conversion of 5-iodo to 5-alkynyl and derived 5-substituted uracil bases and nucleosides" <i>J. Org. Chem.</i> (1983) 48:1854-1862	
	168	RODE "Specificity of thymidylate synthase inactivation by 4,5-bisubstituted dUMP analogues" <i>M. Nencki Inst. Exp. Biol., Acta Biochimica Polonica</i> (1993) 40(3):363-368	
	169	ROGULSKI et al. "Glioma cells transduced with an <i>Escherichia coli</i> CD/HSV-1 TK fusion gene exhibit enhanced metabolic suicide and radiosensitivity" <i>Hum. Gene Ther.</i> (Jan. 1, 1997) 8:73-85	
	170	RONINSON et al. "Amplification of specific DNA sequences correlates with multi-drug resistance in Chinese hamster cells" <i>Nature</i> (June 14, 1984) 309:626-628	
	171	RUTH and BERGSTROM "C-5 substituted pyrimidine nucleosides. 1. Synthesis of C-5 allyl, propyl, and propenyl uracil and cytosine nucleosides via organopalladium intermediates" <i>J. Org. Chem.</i> (1978) 43(14):2870-2876	
	172	SANTI "Perspectives on the design and biochemical pharmacology of inhibitors of thymidylate synthetase" <i>J. Med. Chem.</i> (Feb. 1980) 23(2):103-111	
	173	SASTRY et al. "Membrane-permeable dideoxyuridine 5'-monophosphate analogue inhibits human immunodeficiency virus infection" <i>Mol. Pharmacol.</i> (1992) 41:441-445	
	174	SATYAM et al. "Design, synthesis, and evaluation of latent alkylating agents activated by glutathione S-transferase" <i>J. Med. Chem.</i> (1996) 39:1736-1747	
	175	SAUTER et al. "Heterogeneity of erbB-2 gene amplification in bladder cancer" <i>Cancer Res.</i> (May 15, 1993) 53:2199-2203	

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E. E. Crane

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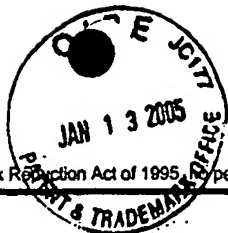
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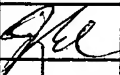

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Sheet 13 of 15

**Complete if Known**

Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 --1615--
Examiner Name	Not Yet Assigned
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	176	SCHIFFER et al. "Crystal structure of human thymidylate synthase: A structural mechanism for guiding substrates into the active site" <i>Biochemistry</i> (1995) 34:16279-16287		
	177	SCHIMKE "Gene amplification in cultured cells" <i>J. Biol.Chem.</i> (May 5, 1988) 263(13):5989-5992		
	178	SCHULTZ et al. "Role of thymidylate synthase in the antitumor activity of the multitargeted antifolate, LY231514" <i>Anticancer Res.</i> (1999) 19:437-444		
	179	SEGOVIA "Leishmania gene amplification: A mechanism of drug resistance" <i>Ann. Trop. Med. Parasit.</i> (1994) 88(2):123-130		
	180	SHEPARD and LEWIS "Resistance of tumor cells to tumor necrosis factor" <i>J. Clin. Immunol.</i> (1988) 8(5):333-341		
	181	SIMON and SCHINDLER "Cell biological mechanisms of multidrug resistance in tumors" <i>PNAS USA</i> (April 1994) 91:3497-3504		
	182	SINGH et al. "Studies on the preparation and isomeric composition of <sup>186</sup> Re- and <sup>188</sup> Re-pentavalent rhenium dimercaptosuccinic acid complex" <i>Nucl. Med. Commun.</i> (1993) 14:197-203		
	183	SLAMON et al. "Human breast cancer: Correlation of relapse and survival with amplification of the HER-2/ <i>neu</i> oncogene" <i>Science</i> (Jan. 9, 1987) 235:177-182		
	184	SLAMON et al. "Studies of the HER-2/ <i>neu</i> proto-oncogene in human breast and ovarian cancer" <i>Science</i> (May 12, 1989) 244:707-712		
	185	SLANSKY and FARNHAM "Transcriptional regulation of the dihydrofolate reductase gene" <i>BioEssays</i> (1996) 18(1):55-62		
	186	SMITH et al. "Regulation and mechanisms of gene amplification" <i>Phil. Trans. R. Soc. Lond. B</i> (1995) 347:49-56		
	187	SNYDMAN et al. "Analysis of trends in antimicrobial resistance patterns among clinical isolates of <i>Bacteroides fragilis</i> group species from 1990 to 1994" <i>Clin. Infect. Dis.</i> (1996) 23(Suppl. 1):S54-S65		
	188	STASCHKE et al. "The in vitro anti-hepatitis B virus activity of FIAU [1-(2'-deoxy-2'-fluoro-1-β-D-arabinofuranosyl-5-iodo)uracil] is selective, reversible, and determined, at least in part, by the host cell" <i>Antiviral Res.</i> (1994) 23:45-61		
	189	STOUT et al. "Structure-based design of inhibitors specific for bacterial thymidylate synthase" <i>Biochemistry</i> (1999) 38:1607-1617		
	190	STÜHLINGER et al. "Clinical therapy and HER-2 oncogene amplification in breast cancer: Chemo vs radiotherapy" <i>J. Steroid Biochem. Molec. Biol.</i> (1994) 49(1):39-42		
		191	SUGARMAN et al. "Recombinant human tumor necrosis factor-α. Effects on proliferation of normal and transformed cells in vitro" <i>Science</i> (Nov. 22, 1985) 230(4728):943-945	

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		Filing Date	November 28, 2002
		First Named Inventor	H. Michael SHEPARD
		Art Unit	1623 --1615--
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<i>[Signature]</i>	192	SUKUMAR and BARBACID "Specific patterns of oncogene activation in transplacentally induced tumors" <i>PNAS USA</i> (Jan. 1990) 87:718-722	
<i>[Signature]</i>	193	TAKEISHI et al. "Nucleotide sequence of a functional cDNA for human thymidylate synthase" <i>Nucl. Acid Res.</i> (1985) 13(6):2035-2043	
<i>[Signature]</i>	194	TANNOCK "Treatment of cancer with radiation and drugs" <i>J. Clin. Oncol.</i> (Dec. 1996) 14(12):3156-3174	
<i>[Signature]</i>	195	TENNANT et al. "Antiviral activity and toxicity of fialuridine in the woodchuck model of hepatitis B virus infection" <i>Hepatology</i> (July 1998) 28(1):179-191	
<i>[Signature]</i>	196	TOLSTIKOV et al. "Synthesis and DNA duplex stabilities of oligonucleotides containing C-5-(3-methoxypropynyl)-2'-deoxyuridine residues" <i>Nucleos. Nucleot.</i> (1997) 16(3):215-225	
**	197	<del>TOWNSEND (eds), Chemistry of Nucleosides and Nucleotides, Vol. 3, Plenum Press, New York, NY (1974) only Table of Contents, Bibliography, pages 529-535 and Index pp. 537-552 supplied</del>	
<i>[Signature]</i>	198	TROUTNER "Chemical and physical properties of radionuclides" <i>Nucl. Med. Biol.</i> (1987) 14(3):171-176	
<i>[Signature]</i>	199	UBEDA and HABENER "The large subunit of the DNA replication complex C (DSEB/RF-C140) cleaved and inactivated by Caspase-3 (CPP32/YAMA) during fas-induced apoptosis" <i>J. Biol. Chem.</i> (Aug. 1, 1997) 272(31):19562-19568	
<i>[Signature]</i>	200	VALETTE et al. "Decomposition pathways and <i>in vitro</i> HIV inhibitory effects of isoddA pronucleotides: Toward a rational approach for intracellular delivery of nucleoside 5'-monophosphates" <i>J. Med. Chem.</i> (1996) 39:1981-1990	
<i>[Signature]</i>	201	van de VIJVER et al. "Amplification of the <i>neu</i> (c- <i>erbB-2</i> ) oncogene in human mammary tumors is relatively frequent and is often accompanied by amplification of the linked c- <i>erbA</i> oncogene" <i>Mol. Cell. Biol.</i> (May 1987) 7(5):2019-2023	
<i>[Signature]</i>	202	van LAAR et al. "Comparison of 5-fluoro-2'-deoxyuridine with 5-fluorouracil and their role in the treatment of colorectal cancer" <i>European J. Cancer</i> (1998) 34(3):296-306	
<i>[Signature]</i>	203	VOLM et al. "Relationship of inherent resistance to doxorubicin, proliferative activity and expression of P-glycoprotein 170, and glutathione S-transferase- <i>π</i> in human lung tumors" <i>Cancer</i> (Aug. 15, 1992) 70(4):764-769	
<i>[Signature]</i>	204	WAHBA and FRIEDKIN "Direct spectrophotometric evidence for the oxidation of tetrahydrofolate during the enzymatic synthesis of thymidylate" <i>J. Biol. Chem.</i> (Mar. 1961) 236(3):C11-C12	
<i>[Signature]</i>	205	WANG et al. "Identification and characterization of Ich-3, a member of the interleukin-1 $\beta$ converting enzyme (ICE)/Ced-3 family and an upstream regulator of ICE" <i>J. Biol. Chem.</i> (Aug. 23, 1996) 271(34):20580-20587	

Examiner's Signature	L. E. Czane <i>[Signature]</i>	Date Considered	09/21/2005
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Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 -- <del>1615</del> --
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

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L. E. Crane

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Sheet 1 of 5

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Examiner Initials*	Cite No. <sup>1</sup>	Document Number Number - Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document Country Code <sup>3</sup> - Number <sup>4</sup> - Kind Code <sup>5</sup> (if known)	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
<i>He</i>	1	DE 32 29 169 A1	02-09-84	De Clercq et al.		
<i>He</i>	2	EP 0 311 107 A2	04-12-89	Stichting REGA VZW		
<i>He</i>	3	EP 0 311 108 A2	04-12-89	Stichting REGA VZW		
<i>He</i>	4	EP 0 316 592	05-24-89	Stichting REGA VZW		
<i>He</i>	5	GB 982 776	02-10-65	The Wellcome Foundation		
<i>He</i>	6	RO 88451	01-30-86	Antibiotics Enterprise, Iasi		X
<i>He</i>	7	WO 89/05817	06-29-89	Nucleic Acid Research Institute		
<i>He</i>	8	WO 90/03978	04-19-90	Stichting REGA VZW		
<i>He</i>	9	WO 91/17424	11-14-91	Vical, Inc.		
<i>He</i>	10	WO 92/19767	11-12-92	Terrapin Technologies, Inc.		
<i>He</i>	11	WO 93/06120	04-01-93	University of Rochester		

Examiner's  
Signature

L. E. Crane

Date  
Considered

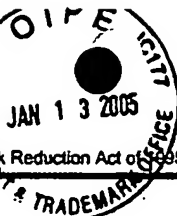
09/21/2005

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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 2 of 5

**Complete if Known**

Application Number	10/048,033
Filing Date	November 27, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 1615 ---
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

**U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Document Number Number - Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
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**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document Country Code <sup>3</sup> - Number <sup>4</sup> - Kind Code <sup>5</sup> (if known)	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
Me	12	WO 94/03467	02-17-94	Institute of Organic Chemistry & Biochemistry of the Academy of Sciences of the Czech Republic, et al.		
**	13	WO 94/22483	10-13-94	Kozak, Alexander		
Me	14	WO 95/01806	01-19-95	Kondratyev, A.		
	15	WO 95/08556	03-30-95	Amersham International, Inc.		
Me	16	WO 95/12678	05-11-95	Connors, T. et al.		
**	17	WO 95/03451	02-08-96	Springer et al.		
**	18	WO 96/07419	04-04-96	University of Georgia Research Foundation & Yale University		

Examiner's  
Signature

L. E. Crane

Date  
Considered

09/21/2005

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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

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Sheet 3 of 5

**Complete if Known**

Application Number	10/048,033
Filing Date	November 27, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 --4615--
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

**U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number - Kind Code <sup>2</sup> (if known)			

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Country Code <sup>3</sup> - Number <sup>4</sup> - Kind Code <sup>5</sup> (if known)				
	19	WO 96/10030	04-04-96	Isis Pharmaceuticals, Inc.		
JRC	20	WO 96/29336	09-26-96	Medical Research Council, University College Cardiff Consultants, Inc. Rega Foundation		
JRC	21	WO 96/33168	10-24-96	Kumiai Chemical Industry Co Ltd et al.		
JRC	22	WO 96/40088	12-19-96	Hostetter, Karl Y.		
	23	WO 96/40708	12-19-96	La Jolla Pharmaceuticals, Inc.		
JRC	24	WO 96/40739	12-19-96	Terrapin Technologies, Inc.		
JRC	25	WO 97/25342	07-17-97	Terrapin Technologies, Inc.		

Examiner's  
Signature

L. E. Crane

Date  
Considered

09/21/2005

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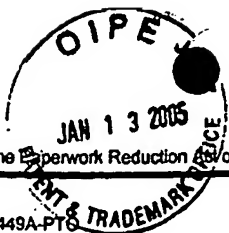
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10/048,033 - PTO-1449 #2

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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

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Sheet 4 of 5

**Complete if Known**

Application Number	10/048,033
Filing Date	November 27, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 ---1615---
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

**U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number - Kind Code <sup>2</sup> (if known)			
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**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Country Code <sup>3</sup> - Number <sup>4</sup> - Kind Code <sup>5</sup> (if known)				
XX	26	WO 97/28179	08-07-97	Flick, James & Israel, Mark		
me	27	WO 97/49717	12-31-97	Balzarini et al.		
me	28	WO 98/49177	11-05-98	University College Cardiff Consultants Limited		
me	29	WO 99/06072	02-11-99	Boehringer Mannheim Corp.		
me	30	WO 99/20741	04-29-99	Geron Corporation		
me	31	WO 99/23104	05-14-99	The Government of the United States of America represented by The Secretary of Health & Human Services		

Examiner's  
Signature L. E. CraneDate  
Considered

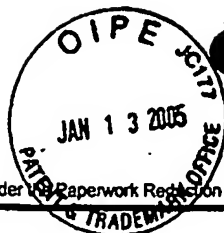
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Approved for use through 07/31/2008. OMB 0851-0031  
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

<b>Substitute for form 1449A-PTO</b>  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)  Sheet 5 of 5				<b>Complete if Known</b>	
				Application Number	10/048,033
				Filing Date	November 27, 2002
				First Named Inventor	H. Michael SHEPARD
				Art Unit	1623 -- <del>1645</del> --
				Examiner Name	Not Yet Assigned
				Attorney Docket Number	NB 2006.01

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Document Number Number - Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document Country Code <sup>3</sup> - Number <sup>4</sup> - Kind Code <sup>5</sup> (if known)	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
	32	WO 99/37753	07-29-99	NewBiotics, Inc.		
	33	WO 00/18775	04-06-00	University College Cardiff Consultants Limited and Rega Foundation		
	34	WO 00/33888	06-15-00	Dubois, V. et al.		
	35	WO 01/07088	02-01-01	NewBiotics, Inc.		
	36	WO 01/83501	11-08-01	University College Cardiff Consultants Limited and Rega Foundation		
	37	WO 01/85749	11-15-01	University College Cardiff Consultants Limited and Rega Foundation		

Examiner's Signature	L. E. Crane <i>[Signature]</i>	Date Considered	09/21/2005
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## ELECTRONIC INFORMATION DISCLOSURE STATEMENT

Electronic Version v18

Stylesheet Version v18.0

p.1 of 2

Title of Invention	METHODS FOR TREATING THERAPY-RESISTANT TUMORS						
Application Number :	10/048033						
Confirmation Number:	2767						
First Named Applicant:	H. SHEPARD						
Attorney Docket Number:	NB 2006.01						
Art Unit:	4616 / 623						
Examiner:	Not Yet Assigned						
Search string:	(3852266 or 4247544 or 4267171 or 4542210 or 4668777 or 4816570 or 4948882 or 4963263 or 4963533 or 4975278 or 5070082 or 5077282 or 5077283 or 5085983 or 5116822 or 5116827 or 5133866 or 5137724 or 5212161 or 5212291 or 5217869 or 5233031 or 5264618 or 5300425 or 5338659 or 5430148 or 5433955 or 5457187 or 5459127 or 5516631 or 5521161 or 5527900 or 5596018 or 5616564 or 5627165 or 5645988 or 5663321 or 5733896 or 5798340 or 5968910 or 5981507 or 6057305 or 6245750 or 6339151 or 6495553 or 20010034440 ).pn						
<b>US Patent Documents</b>							
Note: Applicant is not required to submit a paper copy of cited US Patent Documents							
init	Cite.No.	Patent No.	Date	Patentee	Kind	Class	Subclass
38	1	3862266	1974-12-03	Kiyonagi et al.			
He	2	4247544	1981-01-27	Bergstrom et al.			
9	3	4267171	1981-04-12	Bergstrom et al.			
7	4	4542210	1985-09-17	Sakata et al.			
7	5	4668777	1987-05-26	Caruthers et al.			
7	6	4816570	1989-03-28	Farquhar			
7	7	4948882	1990-08-14	Ruth			
7	8	4963263	1990-10-16	Kauvar			
He	9	4963533	1990-10-16	de Clercq et al.			
He	10	4975278	1990-12-04	Senter et al.			
He	11	5070082	1991-12-03	Murdoek et al.			
He	12	5077282	1991-12-01	Murdoek et al.			
He	13	5077283	1991-12-01	Murdoek et al.			
He	14	5085983	1992-02-04	Scanlon			
He	15	5116822	1992-05-26	De Clercq et al.			
He	16	5116827	1992-05-26	Murdoek et al.			
He	17	5133866	1992-07-28	Kauvar			
He	18	5137724	1992-08-11	Balzarini et al.			
He	19	5212161	1993-05-18	Monniere et al.			
Examiner Name				Date			
L.E. CRANE				09/21/2005			

\*\* Duplicate citations: see PTO-892 for citations.


10/048,033 - PTO-1449 #1

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## ELECTRONIC INFORMATION DISCLOSURE STATEMENT

Electronic Version v18  
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p. 2 of 2

Title of Invention		METHODS FOR TREATING THERAPY-RESISTANT TUMORS					
Application Number :		10/048033					
Confirmation Number:		2767					
First Named Applicant:		H. SHEPARD					
Attorney Docket Number:		NB 2006.01					
Art Unit:		1615		1623			
Examiner:		Not Yet Assigned					
<del>20</del>	<del>5212291</del>	<del>1993-05-18</del>	<del>Murdock et al.</del>				
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<del>23</del>	<del>5264618</del>	<del>1993-11-23</del>	<del>Felgner et al.</del>				
<del>24</del>	<del>5300425</del>	<del>1994-04-05</del>	<del>Kauvar</del>				
<del>25</del>	<del>5338659</del>	<del>1994-08-16</del>	<del>Kauvar et al.</del>				
<del>26</del>	<del>5430148</del>	<del>1995-07-04</del>	<del>Webber et al.</del>				
<del>27</del>	<del>5433955</del>	<del>1995-07-18</del>	<del>Bredehorst et al.</del>				
<del>28</del>	<del>5457187</del>	<del>1995-10-10</del>	<del>Gmeiner et al.</del>				
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<del>30</del>	<del>5516631</del>	<del>1996-05-14</del>	<del>Frisch</del>				
<del>31</del>	<del>5521161</del>	<del>1996-05-28</del>	<del>Malley et al.</del>				
<del>32</del>	<del>5527900</del>	<del>1996-06-18</del>	<del>Balzarini et al.</del>				
<del>33</del>	<del>5596018</del>	<del>1997-01-21</del>	<del>Baba et al.</del>				
<del>34</del>	<del>5616564</del>	<del>1997-04-01</del>	<del>Rapaport et al.</del>				
<del>35</del>	<del>5627165</del>	<del>1997-05-06</del>	<del>Glazier</del>				
<del>36</del>	<del>5645988</del>	<del>1997-07-08</del>	<del>Vande Woude et al.</del>				
<del>37</del>	<del>5663321</del>	<del>1997-09-02</del>	<del>Gmeiner et al.</del>				
<del>38</del>	<del>5733896</del>	<del>1998-03-31</del>	<del>Holy et al.</del>				
<del>39</del>	<del>5798340</del>	<del>1998-08-25</del>	<del>Bischofberger et al.</del>				
<del>40</del>	<del>5968910</del>	<del>1999-10-19</del>	<del>Balzarini</del>				
<del>41</del>	<del>5981507</del>	<del>1999-11-09</del>	<del>Josephson et al.</del>				
<del>42</del>	<del>6057305</del>	<del>2000-05-02</del>	<del>Holy et al.</del>				
<del>43</del>	<del>6246750</del>	<del>2001-06-12</del>	<del>Shepard</del>				
<del>44</del>	<del>6339151</del>	<del>2002-02-15</del>	<del>Shepard et al.</del>				
<del>45</del>	<del>6495553</del>	<del>2002-12-17</del>	<del>Shepard</del>				
<b>** Duplicate citations: see PTO-892 for citations.</b>							
<b>US Published Applications</b>							
Note: Applicant is not required to submit a paper copy of cited US Published Applications							
Init	Cite No.	Pub. No.	Date	Applicant	Kind	Class	Subclass
58	1	20040084440	2004-10-25	Shepard et al.			
<b>Signature</b>							
Examiner Name				Date			
L.E. ORANE				09/21/2005			

\*\* Duplicate citations: see PTO-892 for citations.

10/048,033 - PTO-1449 #1

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